SUPPLEMENTAL MATERIAL

Table S1. Univariable association of IL-6 quintile with outcomes. N and % of cases with the outcome are shown.

	IL-6 quintile					
Outcome	1 (n=606)	2 (n=606)	3 (n=607)	4 (n=606)	5 (n=606)	p-value
Death	79 (13%)	128 (21%)	184 (30%)	219 (36%)	293 (48%)	<0.001
CVD Composite	87 (15%)	117 (22%)	197 (37%)	227 (44%)	263 (55%)	<0.001
CKD Progression	127 (21%)	177 (29%)	203 (33%)	229 (38%)	252 (42%)	<0.001
HGB drop below normal	145 (24%)	223 (37%)	256 (42%)	291 (48%)	334 (55%)	<0.001

CVD Composite= Composite of MI, stroke, PAD, or CHF. CKD Progression= Composite of either a 50% or larger drop in eGFR from baseline or reaching ESRD. HGB decline= HGB decline over time measured using a binary indicator for having a below-normal final HGB value (<11.7 g/dL for women or <12.4 g/dL for men).

Table S2. Univariable association of rs855791 genotype with outcomes.

	rs855791 Genotype			
Outcome	0 (GG) (n=1569)	1 (GA) (n=1122)	2 (AA) (n=340)	p-value
All-cause mortality	503 (32%)	314 (28%)	86 (25%)	0.01
CVD composite	489 (36%)	319 (32%)	83 (28%)	0.007
Renal composite	569 (36%)	337 (30%)	82 (24%)	<0.001
HGB drop below normal	710 (45%)	426 (38%)	113 (33%)	<0.001

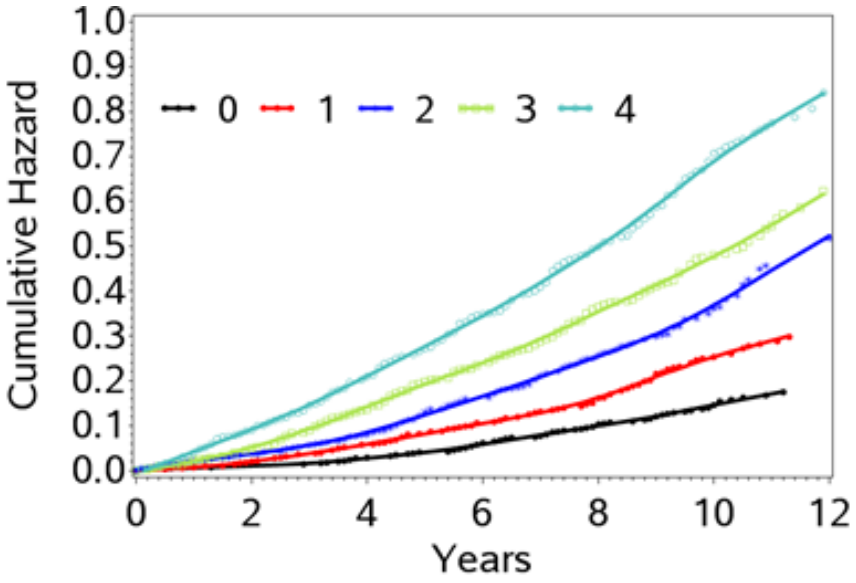
CVD composite= Composite of MI, stroke, PAD, or CHF; Renal= Composite of either a 50% or larger drop in eGFR from baseline or reaching ESRD. HGB decline= HGB decline over time measured using a binary indicator for having a below-normal final HGB value (<11.7 g/dL for women or <12.4 g/dL for men).

Table S3. **Multivariable Cox proportional hazard model that adjusted for genotype only and a model that adjusted for pooled cohort equation 10-year CVD risk, education, UACR, eGFR, population stratification, and if necessary, for non-proportionality.**

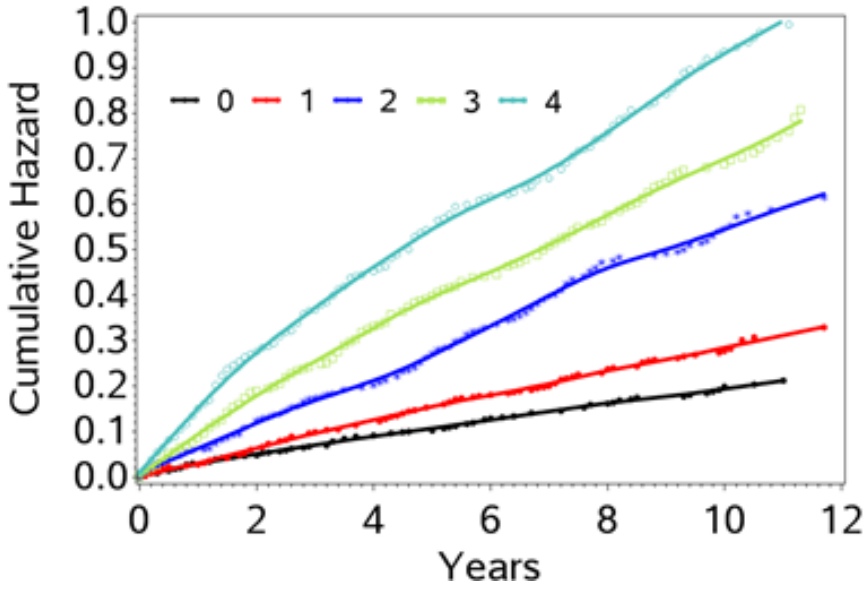
Genotype	**HR (95% CI)** Adjusted for IL-6 and genotype	**p-value**	**HR (95% CI)** Adjusted for all covariates	**p-value**
Death				
GG	Reference		Reference	
AG	0.90 (0.78-1.03)	0.12	1.03 (0.89-1.19)	0.7
AA	0.83 (0.66-1.04)	0.11	1.03 (0.81-1.30)	0.82
CVD Composite				
GG	Reference		Reference	
AG	0.88 (0.77-1.02)	0.08	1.01 (0.87-1.16)	0.92
AA	0.76 (0.60-0.96)	0.02	1.00 (0.79-1.27)	0.99
CKD Progression				
GG	Reference		Reference	
AG	0.79 (0.69-0.90)	<0.001	0.85 (0.74-0.97)	0.02
AA	0.62 (0.49-0.78)	<0.001	0.69 (0.54-0.87)	0.002
HGB Decline				
GG	Reference		Reference	
AG	0.87 (0.77-0.98)	0.022	0.96 (0.85-1.08)	0.47
AA	0.79 (0.65-0.97)	0.023	0.95 (0.78-1.17)	0.64

Figure S1. Cumulative hazard functions for each outcome, stratified by IL-6. These are unadjusted HRs. a) Mortality, b) CVD composite, c) CKD progression, d) hemoglobin decline

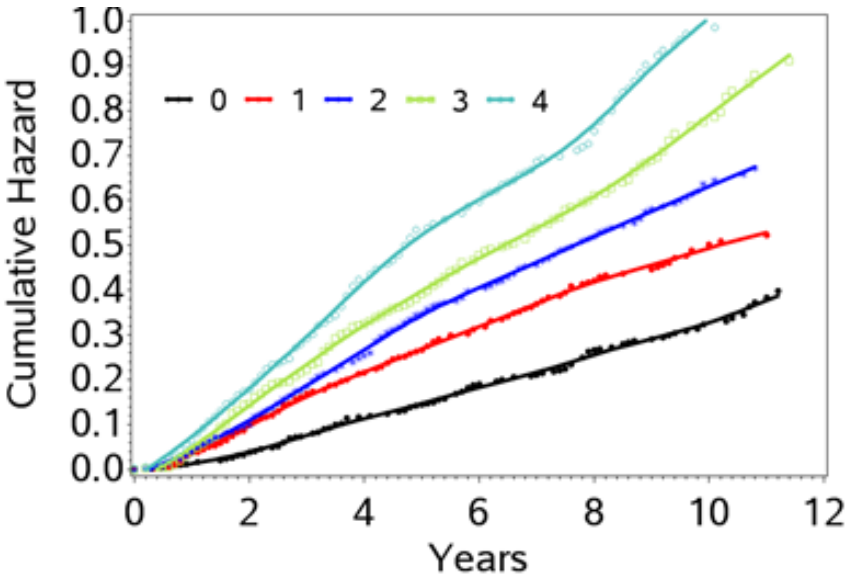
A. Mortality: HR 1.44 (1.37-1.52), p<0.001 per quintile increase



B. CVD composite: HR 1.48 (1.41-1.56), p<0.001 per quintile increase



C. CKD Progression: HR 1.29 (1.23-1.35), p<.0001, per quintile increase



D. HGB decline: HR 1.32 (1.26-1.37) p<.0001, per quintile increase

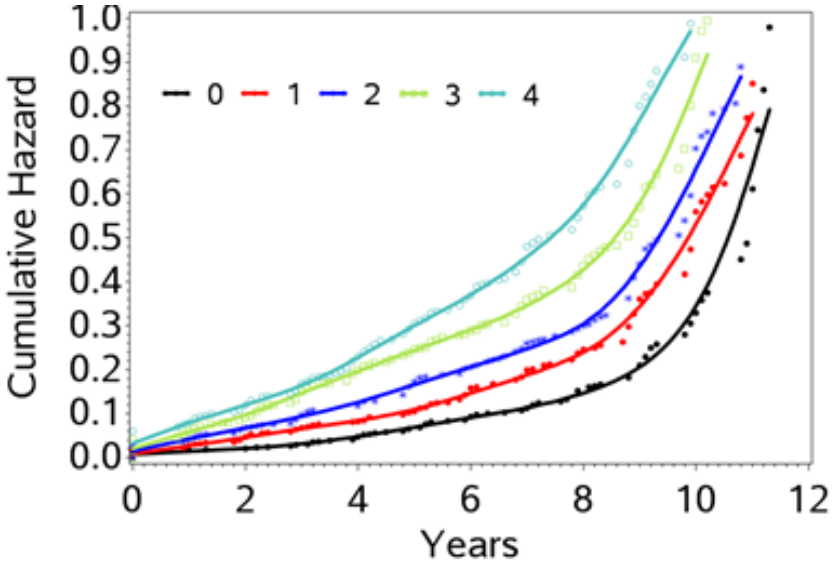
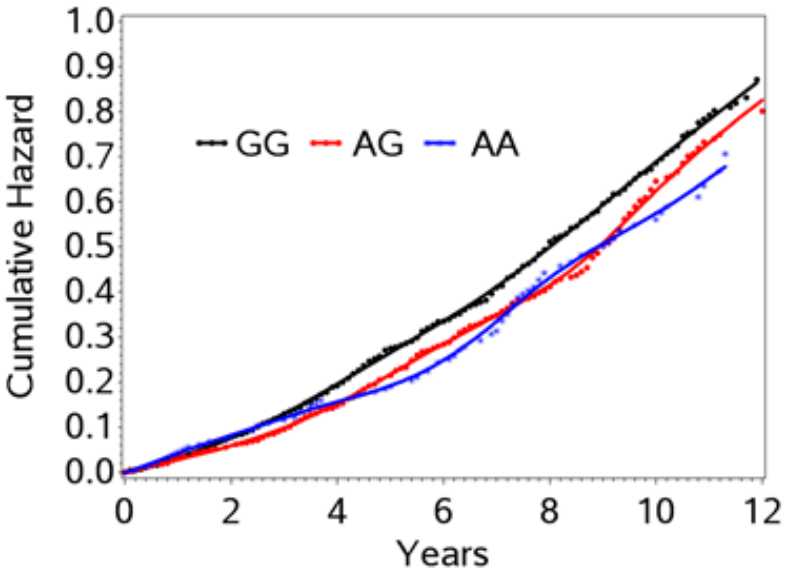
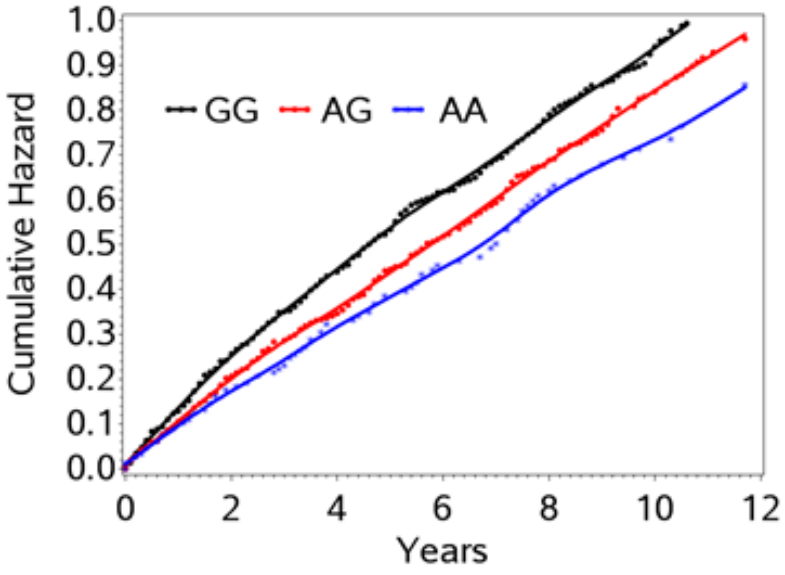


Figure S2. Cumulative hazard functions for each outcome, stratified by genotype only. These are unadjusted HRs. a) Mortality, b) CVD composite, c) CKD progression, d) hemoglobin decline

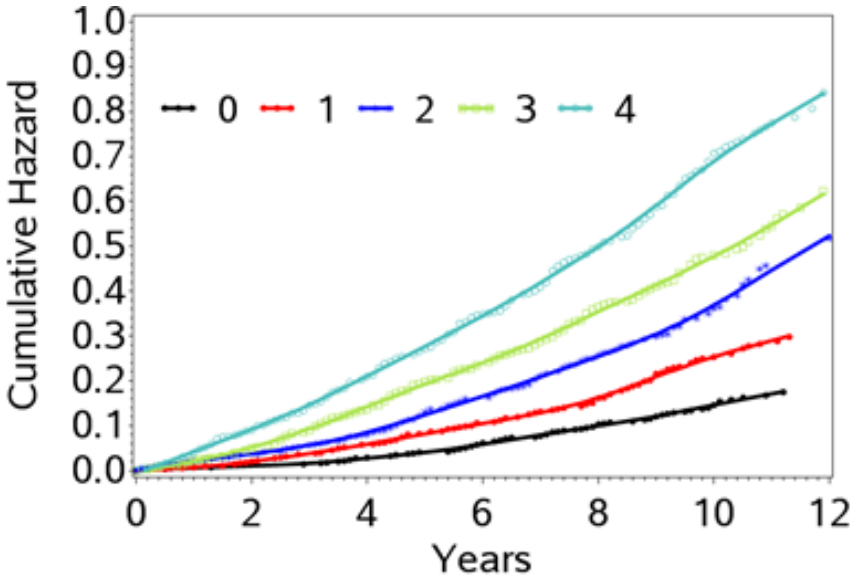
A. Mortality: AG vs GG HR 0.89 (0.78-1.03), p=0.12; AA vs GG HR 0.83 (0.66-1.04), p=0.11



B. CVD composite: AG vs GG HR 0.88 (0.77-1.01), p=0.08; AA vs GG HR 0.76 (0.60-0.96), p=0.03



C. CKD Progression: AG vs GG HR 0.79 (0.69-0.90), p<0.001; AA vs GG HR 0.62 (0.49-0.78), p<0.001



D. HGB decline: AG vs GG HR 0.87 (0.77-0.98), p=0.022; AA vs GG HR 0.79 (0.65-0.97), p=0.023